IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TWINSTRAND BIOSCIENCES, INC. & UNIVERSITY OF WASHINGTON, Plaintiffs/Counterclaim Defendants, v. GUARDANT HEALTH, INC., Defendant/Counterclaim Plaintiff.	C.A. No. 21-1126-GBW-SRF

MEMORANDUM ORDER

In this patent infringement action between Plaintiffs TwinStrand Biosciences, Inc. and the University of Washington (collectively, "Plaintiffs" or "TwinStrand") and Defendant Guardant Health, Inc. ("Defendant" or "Guardant"), Magistrate Judge Fallon held a *Markman* hearing and issued a Report and Recommendation (D.I. 190, the "Report") recommending that the Court adopt constructions for ten agreed upon claim terms and eleven disputed claim terms in U.S. Patent Nos. 10,287,631 ("the '631 patent"), 10,689,699 ("the '699 patent"), 10,752,951 ("the '951 patent"), 10,760,127 ("the '127 patent"), 10,801,063 ("the '063 patent"), 10,889,858 ("the '858 patent"), 11,118,221 ("the '221 patent"), and 11,149,306 ("the '306 patent"). Guardant filed objections (D.I. 198) and TwinStrand responded to those objections (D.I. 215).

The Court has reviewed the Magistrate Judge's Report, the objections and the responses thereto, and has considered *de novo* the original claim construction briefing and supporting documents, as well as the transcript of the claim construction hearing. *See, e.g.*, *St. Clair Intellectual Prop. Consultants, Inc. v. Matsushita Elec. Indus. Co.*, 691 F. Supp. 2d 538, 541-42

(D. Del. 2010); 28 U.S.C. § 636(b)(l); FED. R. CIV. P. 72(b)(3). For the reasons set forth below, Guardant's objections to the Report are **OVERRULED** and the Report is **ADOPTED**.

I. STANDARD OF REVIEW

In reviewing a Magistrate Judge's Report and Recommendation, the Court must "make a de novo determination of those portions of the report or specified proposed findings or recommendations to which objection is made." 28 U.S.C. § 636(b)(1)(C). The Court may "accept, reject, or modify, in whole or in part" the Magistrate Judge's findings or recommendations. *Id.* As to those portions to which no objections have been made, the Court must "satisfy itself that there is no clear error on the face of the record in order to accept the recommendation." FED. R. CIV. P. 72(b) Advisory Committee Notes; *see Henderson v. Carlson*, 812 F.2d 874, 878 (3d Cir. 1987) (explaining the district court's responsibility "to afford some level of review" when no objections have been made).

II. LEGAL STANDARD

"It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (internal quotation marks omitted); *see also Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989) ("A claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using, or selling the protected invention"). "[T]here is no magic formula or catechism for conducting claim construction." *Phillips*, 415 F.3d at 1324. The Court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.* The ultimate question of the proper construction of a patent is a question of law, although

subsidiary fact-finding is sometimes necessary. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837 (2015) (quoting *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996)).

"The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history." *Thorner v. Sony Comput. Ent. Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012) (citing *Phillips*, 415 F.3d at 1312–13). A person of ordinary skill in the art "is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips*, 415 F.3d at 1313.

"When construing claim terms, the court first looks to, and primarily rely on, the intrinsic evidence, including the claims themselves, the specification, and the prosecution history of the patent, which is usually dispositive." *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1276 (Fed. Cir. 2013). "Other claims of the patent in question, both asserted and unasserted, can . . . be valuable" in discerning the meaning of a disputed claim term because "claim terms are normally used consistently throughout the patent," and so, "the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Phillips*, 415 F.3d at 1314. In addition, "[d]ifferences among claims can also be a useful guide[.]" *Id.* For example, "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15.

In addition to the claim, the Court should analyze the specification, which "is always highly relevant to the claim construction analysis ... [as] it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). It is also possible that "the specification may reveal a special definition given to a claim term by the

patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. "Even when the specification describes only a single embodiment, [however,] the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (internal quotation marks omitted) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)). And, the specification "is not a substitute for, nor can it be used to rewrite, the chosen claim language." *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004).

The Court "should also consider the patent's prosecution history, if it is in evidence." *Markman*, 52 F.3d at 980. The prosecution history "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution[.]" *Phillips*, 415 F.3d at 1317.

In some cases, the Court "will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 135 S. Ct. at 841. Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d at 980. Overall, while extrinsic evidence may be useful, it is "less significant than the intrinsic record in determining the legally operative meaning of claim language." *Phillips*, 415 F.3d at 1317 (internal quotation marks and citations omitted).

III. DISCUSSION

As discussed in greater detail below, with respect to those recommendations where neither party has filed an objection, the Court is satisfied that "there is no clear error on the face of the record," *see* FED. R. CIV. P. 72(b) Advisory Committee Notes, and will therefore adopt the Report's recommendations to which there were no objections. Guardant does object to the following recommended claim constructions: (1) the "non-unique" terms (D.I. 190 at 8-14); (2) "degenerate . . . sequence(s)" and "semi-degenerate . . . sequence(s)" (*id.* at 15-20); (3) the "high accuracy" terms (*id.* at 20-23); (4) "fragment features" and "DNA fragment-specific information" (*id.* at 23-25); and (5) "fragment ends" (*id.* at 25-27). D.I. 198 at 1. For the reasons stated below, the Court, having reviewed the record *de novo*, agrees with the Report's conclusions and finds the Magistrate Judge is correct as a matter of law and fact.[1]

A. No Objections to the Magistrate Judge's Report

Neither party filed an objection to the Magistrate Judge's Report (1) adopting the parties' agreed-upon constructions, *see* D.I. 190 at 2, or (2) adopting the plain and ordinary meaning of the disputed term "comprises between 1 nanogram (ng) and 100 ng of cfDNA molecules" in claim 3 of the '221 patent and claim 19 of the '306 patent, *see id.* at 3. Thus, to accept these recommendations from the Magistrate Judge's Report, the Court need only satisfy itself that there "is no clear error on the face of the record." FED. R. CIV. P. 72(b) Advisory Committee Notes.

[1] In its objection, Guardant states, "[t]o the extent that this Court finds that Guardant has not proven indefiniteness during claim construction, Guardant should be allowed to assert indefiniteness later in the proceedings because there is at least a fact dispute." D.I. 198 at 1. The Court will grant Guardant's request—that is, "to the extent appropriate, [Guardant] may raise the issue later or at trial after full fact and expert discovery." *ArcelorMittal v. AK Steel Corp.*, C.A. No. 13-685-MN, 2019 WL 3391814, at *6 (D. Del. July 26, 2019).

Accordingly, the Court agrees with the Report's conclusions. The Court is satisfied that there is no clear error on the face of the record with respect to the parties' agreed-upon constructions and, thus, will adopt the agreed-upon constructions. D.I. 190 at 2. Similarly, with respect to the Report's recommendation that the disputed term "comprises between 1 nanogram (ng) and 100 ng of cfDNA molecules" in claim 3 of the '221 patent and claim 19 of the '306 patent be construed to have its plain and ordinary meaning, the Court agrees and, therefore, adopts the plain and ordinary meaning of this term. The Federal Circuit has consistently interpreted the word "comprises" to be an open-ended term, meaning "that the listed elements (i.e., method steps) are essential but other elements may be added." *Lucent Tech., Inc. v. Gateway, Inc.*, 525 F.3d 1200, 1214 (Fed. Cir. 2008) (citing *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1344-45 (Fed. Cir. 2003)). Importantly, when the word "comprises" appears in the body of the claim and precedes a precise numerical range, the Federal Circuit has rejected attempts to construe such a claim in a manner that exceeds the bounds of the claimed numerical range because such a construction "would read out of [the claim] the express claim ranges." *Jeneric/Pentron, Inc. v. Dillon Co., Inc.*, 205 F.3d 1377, 1382-83 (Fed. Cir. 2000); *see also Wis. Alumni Rsch. Found. v. Apple, Inc.*, 905 F.3d 1341, 1348 n.8 (Fed. Cir. 2008) ("Comprising is not a weasel word with which to abrogate claim limitations.") (quoting *Spectrum Int'l, Inc. v. Sterilite Corp.*, 164 F.3d 1372, 1380 (Fed. Cir. 1998)). Here, as the Report correctly concludes, because the word "comprises" appears in the body of dependent claims and precedes a precisely defined numerical range of 1 to 100 ng of cfDNA molecules, *see, e.g.*, '221 patent at claim 3; '306 patent at claim 19, a person of ordinary skill in the art would understand that the plain and ordinary meaning of the term preserves the specified range as claimed. *See Jeneric*, 205 F.3d at 1381-83; *Takeda Pharm. Co. Ltd. v. Zydus Pharms. USA Inc.*, 743 F.3d 1359, 1364 (Fed. Cir. 2014).

Accordingly, the Court agrees with the Magistrate Judge's recommendation to adopt the parties' agreed-upon constructions and, hereby, adopts the plain and ordinary meaning of the disputed term "comprises between 1 nanogram (ng) and 100 ng of cfDNA molecules" in claim 3 of the '221 patent and claim 19 of the '306 patent.

B. Guardant's Objections to the Magistrate Judge's Report

a. The "non-unique" Terms

1) "Non-unique"

The Report recommends construing "non-uniquely tagged parent polynucleotide(s)" to mean "a population of parent polynucleotide molecules affixed to polynucleotide barcodes, wherein the same polynucleotide barcode sequence is affixed to multiple parent polynucleotide molecules in the [population / sample], and wherein the polynucleotide barcode sequence serves as a molecular identifier only when combined with other information from the tagged parent polynucleotide molecule" and "non-unique tag" to mean "a tag that is affixed to a parent polynucleotide molecule and having a nucleotide sequence, wherein the same tag nucleotide sequence is affixed to multiple parent polynucleotide molecules in the sample, and wherein the tag nucleotide sequence serves as a molecular identifier only when combined with other information from the tagged parent polynucleotide molecule." D.I. 190 at 8-13. In doing so, the Report finds both terms are indefinite. *Id.*

Guardant maintains its objections that these claims are indefinite "because the intrinsic and extrinsic evidence fail to provide any guidance or an objective standard for a [person of ordinary skill in the art ("POSITA")] to determine whether a tag or tagged DNA fragment is 'non-unique' versus 'unique,' i.e., what amount of tag sharing is tolerated before a 'unique' tag or tagged fragment is in fact 'non-unique.'" D.I. 198 at 2. This Court disagrees.

Section 112 of the Patent Act requires that the claims of a patent "particularly point[] out and distinctly claim[] the subject matter which the inventor . . . regards as the invention." 35 U.S.C. § 112(b). The "primary purpose of the definiteness requirement" contained in § 112(b) "is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, *e.g.*, competitors of the patent owner, can determine whether or not they infringe." *All Dental Prodx, LLC v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779-80 (Fed. Cir. 2002).

"A patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014). To determine indefiniteness, courts examine "the patent record—the claims, specification, and prosecution history—to ascertain if they convey to one of skill in the art with reasonable certainty the scope of the invention claimed." *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1341 (Fed. Cir. 2015). While a "'potential infringer'" need not "be able to determine ex ante if a particular act infringes the claims," the patentee must "apprise the public 'of what is still open to them[]'" such that "a person of ordinary skill in the art could determine whether or not an accused product or method infringes the claim." *Niazi Licensing Corp. v. St. Jude Med. S.C., Inc.*, 30 F.4th 1339, 1346-47 (Fed. Cir. 2022) (citations omitted) (internal quotations omitted). The challenger must "prov[e] indefiniteness by clear and convincing evidence." *BASF Corp. v. Johnson Matthey Inc.*, 875 F.3d 1360, 1365 (Fed. Cir. 2017).

Like claim construction, definiteness is a question of law, but the Court must sometimes render factual findings based on extrinsic evidence to resolve the issue of definiteness. *See Sonix Tech. Co. v. Publications Int'l, Ltd.*, 844 F.3d 1370, 1376 (Fed. Cir. 2017). "[A]ny fact critical to

a holding on indefiniteness must be proven by the challenger by clear and convincing evidence." *One-E-Way, Inc. v. Int'l Trade Comm'n*, 859 F.3d 1059, 1062 (Fed. Cir. 2017) (cleaned up).

The Report correctly finds that Guardant has not proven by clear and convincing evidence that these terms are indefinite and that the Report does not "ignore key testimony" or "critical evidence" and is not contradictory. D.I. 198 at 3-4. The hybrid method description informs with reasonable certainty those skilled in the art of the meaning of the "non-unique" terms.[2] The Court agrees with the Report's conclusion that "the 'non-unique' terms can be understood with reasonable certainty in terms of their function, in which shorter n-mer tags are combined with other information from the parent polynucleotide molecule to achieve molecular identification." D.I. 190 at 10 (citation omitted). The Report also addresses Guardant's argument that the "non-unique" terms are indefinite because they do not adequately distinguish between unique and non-unique tagging, and the Court agrees with the Report's conclusions. *Id.* at 10-13.

Accordingly, having reviewed the record *de novo*, the Court agrees with the Report's conclusions regarding the claim terms "non-uniquely tagged parent polynucleotide(s)" and "non-unique tag." Thus, Guardant's objections to these terms are overruled.

2) "Substantially unique"

The Report recommends construing "substantially unique" to have its plain and ordinary meaning and holding that the term is not indefinite. D.I. 190 at 8, 13-14. Guardant maintains its objections that the claim term is "an indefinite term of degree" and does not provide a POSITA "with any guidance of what the metric is, what test you are using, or what is required to be 'substantially unique.'" D.I. 198 at 5-6. The Report did address this argument and the Court

[2] The parties do not dispute that the claimed "non-unique tags" are described in the hybrid method description. D.I. 190 at 9; D.I. 198 at 4-5; D.I. 215 at 1.

agrees with its conclusion. D.I. 190 at 14 ("Because a person of ordinary skill in the art may objectively determine whether a parent polynucleotide molecule is substantially unique by analyzing whether it is differentiated from other parent polynucleotide molecules in the population, this term of degree is not inherently indefinite.").

Having reviewed and considered *de novo* the evidence and arguments advanced by the parties, the Court agrees with the Report's conclusion that Guardant has not shown by clear and convincing evidence that the term "substantially unique" is indefinite. Thus, Guardant's objection to the construction of "substantially unique" is overruled.

b. "Degenerate . . . sequence(s)" and "semi-degenerate . . . sequence(s)"

The Report recommends construing "degenerate . . . sequence(s)" to mean "a nucleotide sequence that is known or unknown in which every nucleotide position is unrestricted in its nucleotide variability" and "semi-degenerate . . . sequence(s)" to mean "a nucleotide sequence that is known or unknown in which at least one, but not all, nucleotide positions are fixed or restricted in their nucleotide variability." D.I. 190 at 15-20. Guardant objects to these constructions as these terms "connotate[] a 'random' DNA sequence." D.I. 198 at 7. The Court disagrees.

The Report correctly concludes that there is no randomization requirement for the degenerate sequences. D.I. 190 at 15-20. The Report states:

> The degenerate and semi-degenerate terms can reasonably be defined based on the variability of the nucleotide positions without imposing the supposedly narrower requirement that those nucleotides must be randomly generated. The word "random" does not appear in the claims. (*See, e.g.*, D.I. 130, Ex. 1 at 39:41-40:31) Instead, it appears only in the specifications' description of "some" embodiments, (*id.*, Ex. 1 at 6:51-53, 7:6-8), or in particular examples or figures set forth in the specification, (*id.*, Ex. 1 at Fig. 2, 20:46-48). The patentees' decision not to modify "degenerate" and "semi-degenerate" sequences with the word "random" in the claims is significant, and it counsels against importing the limitation from the specification into the claims. *See Novartis Pharms. Corp. v. Actavis, Inc.*, C.A. No. 12-366-RGA-CJB, 2013 WL 6142747, at *10 (D. Del. Nov. 21, 2013).

> The specification also fails to support Defendant's position that the nucleotide sequences must always be randomly generated. The '631 patent specification explains that, "[i]n some embodiments, the degenerate or semi-degenerate SMI sequence may be a random degenerate sequence," implying that random generation of the sequence is not required in all embodiments. (D.I. 130, Ex. 1 at 6:51-53); *see Baxalta Inc. v. Genentech, Inc.*, 972 F.3d 1341, 1349 (Fed. Cir. 2020) (concluding that the written description's use of phrases like "may also include," "e.g.," "such as," and "etc." indicated that "the patentee did not intend this excerpt of the written description to define" the disputed term).

Id. at 18.

The Court disagrees with Guardant that the Report is erroneous. Accordingly, having reviewed and considered *de novo* the evidence and arguments advanced by the parties, the Court agrees with the Report's conclusions. Thus, Guardant's objections of the terms "degenerate . . . sequence(s)" and "semi-degenerate . . . sequence(s)" are overruled.

c. The "high accuracy" terms

The Report recommends construing "high accuracy sequence reads" and "high accuracy consensus sequence read" to have their plain and ordinary meaning and finding the claim terms not indefinite. D.I. 190 at 20-23. Guardant objects to these constructions and argues that the Report "is erroneous because it ignores evidence confirming indefiniteness, including that from TwinStrand's own expert" and because it is contradictory. D.I. 198 at 8-9. This Court disagrees.

The Report correctly concludes that a POSITA "would understand that the complementary relationship between the DNA strands is what establishes the claimed method's high accuracy." D.I. 190 at 21. The claims do not require a quantitative accuracy or error rate, as Guardant contends. D.I. 190 at 21; D.I. 198 at 8-9. The Court also does not find the Report contradictory. As TwinStrand correctly points out, the Report merely "observed that the mere presence of a surplus term in the claims does not render" the "high accuracy" terms indefinite and the Report's "discussion of improved accuracy over the prior art" "was simply the observation that the claimed methods will naturally entail results that are better than prior art methods." D.I. 215 at 6.

Having reviewed the record *de novo*, the Court agrees with the Report's conclusions and finds that Guardant has not proven by clear and convincing evidence that the "high accuracy" terms are indefinite. Thus, Guardant's objections are overruled.

d. "Fragment features" and "DNA fragment-specific information"

The Report recommends construing "fragment features" and "DNA fragment-specific information" to have their plain and ordinary meaning. D.I. 190 at 23-25.[3] The Report also finds these terms are not indefinite. *Id.*

Guardant objects to the Report's construction of these terms asserting they are indefinite because a POSITA would not be able to discern the scope of the claims. D.I. 198 at 9-10. Specifically, Guardant argues that the Report "fails to address what DNA sequence information would fall in or outside the scope of the claims." *Id.* at 10 (emphasis in original). Guardant, however, did not raise this argument before the Magistrate Judge and "has not shown good cause for raising new arguments in its Objections that it did not present to the Magistrate Judge." *CoolTVNetwork.com, Inc. v. Blackboard Inc.*, C.A. No. 19-291-LPS-JLH, 2021 WL 2010579, at *1 (D. Del. May 20, 2021) (declining to consider arguments raised for the first time in objections to a report and recommendation); *see also* D.I. 129 at 32-35. Nevertheless, the Court has reviewed the record *de novo* and agrees with the Report's conclusions.

e. "Fragment ends"

The Report recommends construing "fragment ends" to have its plain and ordinary meaning, which is "the distal or terminal part of the fragment." D.I. 190 at 25-27. Guardant

[3] The parties agree that a "fragment" "is a piece of a larger nucleic acid molecule containing the four nitrogenous bases of DNA: adenine ('A'), guanine ('G'), thymine ('T'), and cytosine ('C')." D.I. 190 at 23. The Report notes that the plain and ordinary meaning of "fragment features" means the claimed "features," and the plain and ordinary meaning of "DNA fragment-specific information" means "information are limited to 'DNA sequence information.'" *Id.*

objects to this construction and argues that "fragment ends" "requires shearing/fragmentation (to create diverse shear points for use in unique tagging) and trimming (to achieve the reduced error rate central to the claimed invention)." D.I. 198 at 10. This Court disagrees.

The Court agrees with the Report that there is no requirement that the fragment ends *must* result from shearing and trimming. Rather, as correctly noted in the Report, the specification uses permissive language like "may" when describing shearing of fragment ends, which suggests the fragment ends need not necessarily result from shearing. D.I. 190 at 26 (citing D.I. 130, Ex. 1 at 15:10-12). With respect to trimming, Guardant's construction improperly imports limitations from the specification into the claims. *See Ericsson, Inc. v. D-Link Sys. Inc.*, 773 F.3d 1201, 1218 (Fed. Cir. 2014); *see also* D.I. 190 at 27. Moreover, nothing in the intrinsic record of the '631 patent suggests that the patentees intended to limit the claim scope of "fragment ends."

Accordingly, having reviewed the record *de novo*, the Court agrees with the Report's conclusion that "fragment ends" be construed to have its plain and ordinary meaning. Thus, Guardant's objection is overruled.

* * *

NOW THEREFORE, IT IS **HEREBY ORDERED** on June 2, 2023 that:

1. Guardant's Objections (D.I. 198) to the Report are **OVERRULED**;
2. The Report is **ADOPTED**; and
3. No later than June 9, 2023, the parties shall submit for the Court's signature a Claim Construction Order consistent with this Memorandum Order.

GREGORY B. WILLIAMS
UNITED STATES DISTRICT JUDGE